Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1 -71 (canceled).

72 (Withdrawn). An isolated enzyme capable of mediating a site-specific recombination between two predetermined recombination sites, wherein at least one recombination site is an asymmetric recombination site.

73 (Withdrawn). The isolated enzyme according to claim 72, wherein the recombination is selected from a group consisting of: inversion of a first DNA molecule encompassed within a second DNA molecule, excision of a first DNA molecule from a second DNA molecule, insertion of a first DNA molecule into a second DNA molecule and translocation between a first DNA molecule and a second DNA molecule, wherein the second DNA molecule is selected from the group consisting of: genomic DNA and circular DNA.

74 (Withdrawn). The isolated enzyme according to claim 73, wherein the second DNA molecule is genomic DNA and the first DNA molecule is integrated into a predetermined genomic site selected from the group consisting of: 3’ UTRs, 5’ UTRs, polyA sites and gene promoters.

75 (Withdrawn). The isolated enzyme according to claim 72, wherein said isolated enzyme is a Cre or FLP mutant

mediating recombination between two recombination sites, such that at least one recombination site is an asymmetric recombination site comprising a spacer sequence selected from the group consisting of: SEQ ID NOS. 1-34.

76 (Withdrawn). A plurality of isolated enzymes capable of mediating site-specific recombination between two predetermined recombination sites, wherein at least one of the recombination sites is an asymmetric recombination site, wherein at least one enzyme is selected from the group consisting of: a wild type recombinase, Cre and Flp mutant, and at least one recombination site is an asymmetric recombination site comprising a spacer sequence selected from the group consisting of: SEQ ID NOS. 1-34.

77 (Withdrawn). An isolated polynucleotide encoding the at least one enzyme of claim 76, wherein said isolated polynucleotide is encompassed in a recombinant vector that expresses the at least one recombinase and is selected from the group consisting of: naked DNA plasmid, a plasmid within a liposome, a retroviral vector, an AAV vector, or a recombinant adenoviral vector.

78 (Withdrawn). The isolated polynucleotide according to claim 77, wherein the recombinant vector further comprising a promoter derived from bacteria, yeast, insect, animal, plant and virus and selected from the group consisting of: E. coli *lac* and *trp* operons, the *tac* promoter, the bacteriophage $_{\lambda}$L promoter, bacteriophage T7 and SP6 promoters, β-actin promoter, insulin promoter, human

cytomegalovirus (CMV) promoter, HIV-LTR, RSV-LTR, SV40 promoter, baculoviral polyhedrin and p10 promoter.

79 (Withdrawn). The isolated polynucleotide according to claim 78, wherein the promoter is an inducible promoter selected from the group consisting of: tetracycline, heat shock, steroid hormone, heavy metal, phorbol ester, adenovirus E1A element, interferon and serum inducible promoters.

80 (Withdrawn). The isolated polynucleotide according to claim 77, wherein said isolated polynucleotide encodes a plurality of enzymes, the plurality of enzymes is capable of mediating site-specific recombination between two predetermined recombination sites, wherein at least one of the recombination sites is an asymmetric recombination site and each of the plurality of recombinases recognizes at least one half of the at least one asymmetric recombination site.

81 (Withdrawn). A host cell comprising the polynucleotide of claim 77.

82 (Withdrawn). A genetically modified cell transformed by a site-specific recombination between two recombination sites carried out by the isolated enzyme of claim 72, wherein at least one of the recombination sites is an asymmetric recombination site, and wherein the asymmetric recombination is selected from the group consisting of: inversion, excision, insertion and translocation, wherein the recombination occurs between the cellular endogenous genome and an exogenous DNA molecule such that the exogenous DNA

molecule is integrated by recombination between the two recombination sites into a predetermined locus within the cellular genome.

83 (Withdrawn). The genetically modified cell according to claim 82, wherein said genetically modified cell is eukaryotic, wherein said genetically modified cell is selected from the group consisting of: yeast, plant cell, embryonic stem cell, mesenchymal cell, and haematopoietic progenitor cell.

84 (Withdrawn). A transgenic organism comprising the genetically modified cell of claim 83, said transgenic organism is selected from the group consisting of: plant, yeast and mammal.

85 (Withdrawn). The genetically modified cell according to claim 83, wherein said cell is devoid of an endogenous polynucleotide sequence at a predetermined genomic locus.

86 (Previously presented). A method for treating a disease, comprising:

a. providing a composition comprising a DNA molecule comprising a nucleotide sequence encoding at least one enzyme, the at least one enzyme is capable of mediating site-specific excision of a gene fragment flanked between two recombination sites, wherein at least one recombination site is an asymmetric recombination site;

b. administering the composition to a subject in need thereof; thereby obtaining site-specific excision of the gene fragment from a predetermined genomic locus.

wherein the composition further comprises a carrier operably connected to the isolated DNA molecule, the carrier capable of targeting said isolated DNA molecule to a cell and promoting internalization of said isolated DNA molecule into the cell and said carrier is selected from the group consisting of: viruses, liposomes, lipid/DNA complexes, micelles, protein/lipid complexes, nanoparticles, and microparticles.

87 (Withdrawn). The method according to claim 86, wherein the two recombination sites are the same asymmetric recombination sites.

88 (Withdrawn). The method according to claim 86, wherein the nucleotide sequence encodes a plurality of enzymes capable of catalyzing the recombination.

89 (Withdrawn). The method according to claim 86, wherein the excised gene fragment is a fragment of HIV genomic DNA.

90 (Withdrawn). The method according to claim 86, wherein the composition comprises a recombinant vector encompassing an expression cassette comprising the nucleotide sequence, wherein the vector is selected from the group consisting of: naked DNA plasmid, a plasmid within a liposome, retrovirus, lentivirus, adenovirus, herpes simplex

viruses (HSV), cytomegalovirus (CMV), and adeno-associated virus (AAV).

91 (Previously presented). The method of claim 86, comprising:

a. providing a composition comprising a DNA molecule comprising a nucleotide sequence encoding at least one enzyme, the at least one enzyme is capable of mediating site-specific excision of a gene fragment flanked between two recombination sites at a defined genomic locus, wherein at least one recombination site is an asymmetric recombination site;

b. transforming a cell with the composition; and

c. proliferating the transformed cells ex vivo.

wherein the cell is autologous.

92 (Previously presented). The method according to claim 91, further comprising: selecting cells devoid of said gene fragment and transplanting the selected cell into a subject in need thereof.

93 (Previously presented). The method according to claim 91, wherein transforming the cell with said composition is carried out by a procedure selected from the group consisting of: calcium phosphate transfection, DEAE-dextran mediated transfection, transvection, microinjection, cationic lipid-mediated transfection, electroporation, scrape loading,

ballistic introduction or infection, use of a gene gun and liposome transfection.

94 (Withdrawn). The method of claim 86 wherein the composition comprises a first DNA molecule comprising a first recombination site; and a second DNA molecule comprising a nucleotide sequence encoding at least one enzyme, the at least one enzyme mediates insertion of the first DNA molecule or fragments thereof into a third DNA molecule comprising a second recombination site, wherein the third DNA molecule is genomic DNA such that the first DNA molecule is inserted into a defined locus of the genome selected from the group consisting of: 3' UTRs, 5' UTRs, polyA sites and gene promoters.

95 (Withdrawn). The method according to claim 94, wherein the first DNA molecule comprises a nucleotide sequence consisting of a fragment of human genomic DNA encoding for a molecule selected from the group consisting of: a structural protein, an enzyme and a regulatory molecule.

96 (Withdrawn). The method according to claim 94, wherein the composition further comprises a carrier operably connected to the first and second DNA molecules, the carrier capable of targeting said first and second DNA molecules to a cell encompassing the third DNA molecule, wherein the carrier is selected from the group consisting of: viruses, liposomes, lipid/DNA complexes, micelles, protein/lipid complexes, nanoparticles and microparticles.

97 (Withdrawn). The method according to claim 94, wherein the first DNA molecule and the second DNA molecule are operatively linked to one another and the second DNA molecule is operably linked to a promoter.

98 (Withdrawn). The method according to claim 94, wherein the first DNA molecule comprises a recombination site comprising SEQ ID NO:37 and the second DNA molecule comprising a nucleotide sequence encoding at least one enzyme selected from the group consisting of: wild type Cre, CM1 Cre mutant and CM2 Cre mutant.

99 (Withdrawn). The method according to claim 94, further comprising selecting cells comprising the first DNA molecule integrated within their genome at a predetermined locus and transplanting the cell into a subject in need thereof.

100 (Withdrawn). The method according to claim 86, wherein the composition comprises:

(i) a first DNA molecule, the first DNA molecule comprises a first recombination site; and

(ii) at least one enzyme capable of mediating site-specific insertion of the first DNA molecule into a second recombination site within a specific genomic locus, wherein at least one of said first and second recombination site is an asymmetric recombination site

thereby obtaining at step (b) a site-specific excision of the gene fragment from a predetermined genomic locus.

101 (Withdrawn). The method according to claim 100, wherein the first DNA molecule comprises a recombination site comprising SEQ ID NO:37 and the at least one enzyme is selected from the group consisting of: wild type Cre, CM1 Cre mutant and CM2 Cre mutant.

102(New). The method according to claim 91, wherein the excised gene fragment is a fragment of HIV genomic DNA.